ATOPIC ECZEMA/DERMATITIS

INTEGRATION OF HUMAN EPIDERMAL CHROMOSOMAL INTERACTIONS REVEALS NOVEL CANDIDATE GENES AND LONG-RANGE INTERACTIONS WITH RELATED AD RISK LOCI

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Background: Atopic dermatitis (AD) is a common inflammatory skin disease caused by interaction of polygenic background and environmental factors. Many Genome-wide association studies (GWAS) have been apply to identify and explore candidate gene loci associated with AD. However, the majority of the GWAS SNPs reside in non-coding regions of the genome, leaving the mechanisms of these SNPs remain unknown. Recently, the emerging technology of promoter capture Hi-C (CHi-C) allows high-resolution analysis of physical interactions between regulatory elements and target genes, providing reasonable mechanism and evidence that how the SNPs interact with targeted genes.

Objective: To obtain a better view of the mechanisms of these SNPs of GWAS and explore new driver genes of AD.

Materials and Methods: We selected reported AD-associated SNPs by literature retrieval. Enhancer-promoter interaction loops of the human epidermal cell genome was identified in the capture Hi-C database [PMID: 28805829]. Different expressed genes (DEGs) between lesional skin and normal skin were obtained by processing 8 microarray dataset. We also test for associations between levels of expression and SNP genotype (eQTLs). The interaction between SNP and genes has also been verified by 3C (chromosome conformation capture) experiments in the HaCaT cell line.

Results: 64 reported AD-associated SNPs were identified in 17 published GWAS studies. 14 SNPs have long-range physical interaction (>100 kb) with genes using CHi-C data. We also have analysed 8 microarray datasets and yielded 2207 significant DEGs. 11 SNPs were found interacting with the DEGs. Interestingly, 2 SNPs were verified by eQTLs. They are rs12081541 interacting with FLG and rs176095 interacting with HLA-DQB2. Those results have also been verified by 3C experiments.

Conclusions: We found new risk genes and explained the mechanisms of 2 SNPs

interacting with DEGs. We obtained a new method to reveal the pathogenesis of disease.